claims.

REMARKS

Claims 6-13 are currently pending in the present application. The claims have been amended in the expectation that the amendments will place this application in condition for allowance. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

1. Objection to the Information Disclosure Statement

The Official Action states that the Information Disclosure Statement is objected to for the following reasons:

> It is noted that the reference (AC) as cited in PTO-1449 **missing the date and the pertinent pages.** In order to have the reference printed on such resulting patent, a separate listing, preferably on a PTO-1449 form including the Authors, Title, date, publisher, Edition or volume and pertinent pages must be listed on a PTO-1449 and a copy of those references must provide to the office.

Applicants submit that Reference AC on the PTO-1449 filed on January 12, 2001 was correctly cited. In particular, the Examiner requested the citation of the pertinent pages. However, the cited reference is a Chemical Abstract document containing no page numbers. Accordingly, it is impossible for applicants to cite page numbers to the Examiner which do not exist.

Additionally, the Examiner obviously considered the reference to be properly cited as the Examiner both initialed the reference on the PTO-1449 form returned to applicants, as

well as included the reference in the rejection under 35 U.S.C. 103(a), as discussed below. Accordingly, applicants are uncertain as to the nature of the Examiner's objection.

2.Objection to the First Line of the Specification

The Official Action states that the first line of the specification is objected to for the following reasons:

> Applicant should amend the first line of the specification to indicate the status of the priority documents, i.e., This application is a 371 of PCT/IL98/00592, filed 12/07/1998 and claims benefit of Foreign Application Israel 122490, filed 12/07/1997. See MPEP 1302.04.

Applicants thank the Examiner for her suggestion regarding the specification. Accordingly, applicants have amended the first line of the instant specification in accordance with the Examiner's suggestion as found in the enclosed Appendix A.

Regarding the Examiner's citation to MPEP 1302.04, applicants note that this section of the MPEP relates to "Examiner's Amendments and Changes". Accordingly, applicants are uncertain how this section of the MPEP bears any relevance to applicants amendments to the specification to include a recitation of the priority documents.

3. Objection to the Declaration

The Official Action states that the declaration is objected to for the following reasons:

> The declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and

> filing date is required. See MPEP § § 602.01 and 602.02.
> The declaration is defective because:
> The words are **not** legible.

Applicants thank the Examiner for her suggestions regarding the declaration. A new declaration is enclosed herewith in compliance with 37 CFR 1.67(s).

4. Objection to the Specification

The Official Action states that the Specification is objected to for the following reasons:

> Appropriate correction in the specification is required. The page numbering is duplicate (See page 3).
> The specification is objected to because of the following: (1) the page numbering is not consecutively numbered due to a duplicate page 3; (2) the references are not listed on a PTO-1449 and (3) a copy of those references have not been provided to the office.

Applicants respectfully traverse this objection. There are no duplicate page 3's; accordingly, the page numbering is consecutively numbered. In particular, applicants submitted a copy of the PCT publications containing original, consecutively numbered pages 1-16; and amended pages 2, 3, 8, 12, 13, 14, 15, and 16 properly filed under Article 34 of the PCT in Response to the Written Opinion dated September 30, 1999 on February 14, 2000. The Examiner's attention in this regard is directed to Section 1 of the International Preliminary Examination Report dated September 15, 2000 stating that "The amendments filed with

the letter of 14. 02.2000 meet the requirements of Article 34(b) PCT." Further, on the Transmittal Letter filed with the instant application, applicants pointed out to the Examiner that the "PCT/IPEA/409 International Preliminary Examination Report with Amended Sheets (specification and claims) to be examined". Accordingly, there is no duplicate page 3 in the present application.

Regarding the recitation of the references in the specification, these references are meant for the purpose of understanding the background of the invention. Accordingly, we are in the process of ordering and/or reviewing them for materiality and those that are will be cited. The Examiner is reminded that under MPEP 608.01(c), it is proper for applicant to include "references to specific prior art or other information where appropriate." Accordingly, the instant specification does not require any correction.

5. Rejection of Claims 7, 8, and 11-12 under 35 U.S.C. § 112, 2d paragraph

The Official Action states that claims 7, 8, and 11-12 are rejected under 35 U.S.C. § 112, second paragraph for the following reasons:

> Claims 7, 8, 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the

invention.
The phrase "an active component" as recited in claims 7 and dependent claims 11 has no antecedent basis in the claim.
The phrase, "a positive result being a reaction above that which is observed in non-schizophrenic subjects" as recited in claims 7-9 and 11-13 is indefinite and ambiguous as the metes and bounds of the claimed invention. As written in the claims, one of ordinary skill in the art can not appraise the metes and bounds of the claimed invention. This rejection could be overcome by reciting the condition on pages 10 and 13, including the diameter of the wheel at the site of injection.
The phrase "an/or" as recited in claims 8 and dependent claim 11 is not appropriate in the claims. It is suggested that applicants amend the claims to recite either "and" or "or".
Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

Applicants respectfully traverse this rejection. Regarding the §112, second paragraph rejection, caselaw has defined two requirements under the statute: (1) whether the applicant has stated the invention as something elsewhere in the application which would not fall under the scope of the claims; and (2) whether the claims would be communicated with a reasonable degree of particularity and distinctness to a person skilled in the art in light of the content of the disclosure and the teachings of the prior art. MPEP §2171, §2173, and §2173.02.

Applicants thank the Examiner for her suggestions regarding the claims. Accordingly, applicants have amended claim 7 to remove the term "as an active component"; and amended claim 8 to replace the term "and/or" with the term "or".

Regarding the term "a positive result being a reaction above that which is observed in non-schizophrenic subjects" in claims 7-9, applicants respectfully submit that this term is clear. In particular, the original specification as filed states in Table 1 on page 10 that the results of the skin test are reported in terms of "positive", "borderline", or "negative". Additionally, page 8 of the instant specification makes clear that the test used for the DTH (delayed type hypersensitivity) activity being tested is known in the art. (See page 8, lines 10-13). Accordingly, this term is clear.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 7, 8, and 11-12.

6. Rejection of Claims 6-13 under 35 U.S.C. § 103(a)

The Official Action states that claims 6-13 are rejected under 35 U.S.C. § 103(a) as being obvious over Shinitzky et al. (WO 97/13152) and Kessler et al. (Dementia 6(6): 330-3; 1995) and in view of Burbaea et al. (ZH Nevropatol Psikhiatr IM S S Korsakova 86(1); 103-105; 1986).

As the basis of this rejection, the Official Action states:

> Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shinitzky *et al.* (WO 97/13152, PTO 1449) and Kessler et al (Demenita 6(6): 330-3; 1995; PTO 892) and in view of Burbaea *et al* (ZH Nevropatol Psikhiatr IM S S Korsakova 86(1): 103-105; 1986).
> Shinitzky *et al.* (PTO 1449) teach a method of preparing a reagent for use in diagnosing dermantia by collecting blood from a number of individuals,

isolating platelet from the blood samples (See entire document, page 8 in particular) and preparing platelet proteins by isoelectric focusing (See page 10) wherein said proteins have a pI within the range of above about 6.5 to about 9.5 (See page 12. Fig 4).
Shinitzky *et al.* (PTO 1449) differs from the claimed invention preparing platelet protein from individuals with Alzheimer-type dementia.
Kessler *et al* (PTO 892) teach that platelet proteins from young 21-year old schizophrenic patients have an increase in the number of dense granule per platelet with characteristics similar to platelets of 37-year old healthy individuals (See entire document, page 332, Fig. 2, Table 2, and right column). Furthermore, the platelet cell size in schizophrenic patients increases compared with age match healthy controls (See abstract in particular).
Burbaea *et al.* teach the use of delayed type hypersensitivity reaction (DTH) to neuroproteins in schizophrenic patients (See abstract in particular).
Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use delayed type hypersensitivity reaction as taught by Burbaea to diagnose schizophrenia using the platelet proteins as taught by Shinitzky and Kessler. One having ordinary skill in the art would have been motivated to use proteins from platelet to screen the population with psychiatric disorders such as schizophrenia because platelets of schizophrenics are definitively different than normal individual as taught by Kessler.

Applicants respectfully traverse this rejection. The references of record do not teach or suggest applicants' inventive subject matter as a whole as recited in the claims. The Examiner has failed to establish a *prima facie* case of obviousness against the presently rejected claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, the prior art relied

upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art reference must teach or suggest all the limitations of the claims. *In re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

The Shinitzky et al. reference relates to assays for the diagnosis of Alzheimer's type dementia. In particular, the assay relies on obtaining a blood sample from an individual, determining the level of a platelet associated antibody against a 75 kD platelet-protein in said sample, and comparing that level to a control sample. A level higher than that of the control sample indicates that the individual has a high likelihood of having Alzheimer's type dementia.

The Kessler et al. reference states that the numbers of platelet dense granules and platelet cell size in schizophrenic patients increase compared to age-matched healthy controls. In contrast, in patients with Alzheimer's type dementia, the number of platelet dense granules decreases compared to healthy persons.

The Burbaea et al. reference relates to the body sensitization of schizophrenic patients to neurospecific proteins S-100 and 10-40-4. The reference found that there were statistically significant differences in manifestations of delayed type hypersensitivity reaction to these proteins in schizophrenic patients vs. normal subjects.

In contrast, the presently pending claims relate solely to diagnostic methods for determining schizophrenia in a subject comprising obtaining a preparation comprising platelet derived proteins, injecting said preparations into a subject, and examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of the injection. None of the references cited by the Examiner, taken alone or in combination, disclose each and every critical element of the presently claimed invention.

In particular, Shinitzky et al. specifically use a determination of a level of a 75 kD platelet-protein in a blood sample to ascertain whether the patient has Alzheimer's type dementia. Additionally, Kessler et al. measure the number of platelet dense granules and platelet cell size to determine whether a patient is schizophrenic. Further, Burbaea et al. measure the sensitivity of patients to neurospecific proteins S-100 and 10-40-4 to determine whether the patients are schizophrenic. Accordingly, none of the references, taken alone or in combination, teach or suggest a method for determining

schizophrenia in a patient by injecting platelets into the patient and determining whether there is a delayed type hypersensitivity reaction at the site of the injection. Accordingly, each and every element of the presently claimed invention is not disclosed by at least one of the cited references as required by *In re Wilson*.

Additionally, a person of ordinary skill in the art would have had no motivation to combine the cited references to arrive at the presently claimed invention. In particular, the Shinitzky et al. reference related to assays for determining Alzheimer's type dementia in a patient. However, the abstract of the Kessler et al. reference predicts that a patient having Alzheimer's type dementia would exhibit physical characteristics (i.e. number of platelet dense granules) exactly opposite to a patient having schizophrenia. Accordingly, Kessler et al. teach away from using a reference relating to the identification of Alzheimer's type dementia (Shinitzky et al.) to arrive at the presently claimed invention relating to the identification of schizophrenia. The presently claimed invention, therefore, is unobvious over Shinetzky et al. and Kessler et al. in view of Burbaea et al.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 6-13.

CONCLUSION

Claims 6-13 are currently pending in the present

application. Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections and allow all remaining claims herein.

Respectfully submitted,

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BOX PATENT
Attorney Docket No. 24259

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

SHINITZKY et al.

Examiner: P. Huynh

Serial No.: 09/555,964

Art Unit: 1644

Filing Date: September 8, 2000

For: **SKIN TEST FOR SCHIZOPHRENIA**

Appendix A

Please amend the specification as indicated below.

Page 1, line 1, please insert the following paragraph:

B1

--This application is a 371 of PCT/IL98/00592, filed December 7, 1998, and claims the benefit of foreign application IL 122490, filed December 7, 1997.--

BOX PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

SHINITZKY et al. Examiner: P. Huynh

Serial No.: 09/555,964 Art Unit: 1644

Filing Date: September 8, 2000

For: **SKIN TEST FOR SCHIZOPHRENIA**

Appendix B

Please amend the following claims as indicated in the following marked up copy of the claims.

7. (Once Amended) A diagnostic method for determining schizophrenia in a subject comprising:

(a) obtaining a preparation comprising**[**, as an active component,**]** platelet derived proteins or fractions thereof having a pI above about 6.5;

(b) injecting said preparation into a subject; and

(c) examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of the injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic.

8. (Once Amended) A diagnostic method for determining schizophrenia in a subject comprising:

(a) obtaining a blood sample from a number of schizophrenic [and/or] or non schizophrenic individuals other than the tested subject and collecting platelets therefrom;

(b) preparing a protein fraction from said platelet separation comprising proteins or fractions thereof having a pI of about 6.5;

(c) injecting said protein preparation into a subject; and

(d) examining the subject for the occurrence of a delayed type hypersensitivity reaction at the site of the injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic.

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Art Unit: 1644

Filing Date: September 8, 2000

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Appendix C

Please amend the following claims as indicated in the following clean copy of the claims.

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7. (Once Amended) A diagnostic method for determining schizophrenia in a subject comprising:

(a) obtaining a preparation comprising platelet derived proteins or fractions thereof having a pI above about 6.5;

(b) injecting said preparation into a subject; and

(c) examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of the injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic.

8. (Once Amended) A diagnostic method for determining schizophrenia in a subject comprising:

(a) obtaining a blood sample from a number of

schizophrenic or non schizophrenic individuals other than the tested subject and collecting platelets therefrom;

(b) preparing a protein fraction from said platelet separation comprising proteins or fractions thereof having a pI of about 6.5;

(c) injecting said protein preparation into a subject; and

(d) examining the subject for the occurrence of a delayed type hypersensitivity reaction at the site of the injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic.